Please cancel Claims 33-34 as drawn to non-elected inventions without prejudicing the right to file divisional applications thereon.

REMARKS

In view of the amendments and remarks that follow, Applicants respectfully submit that the application is in condition for allowance. Accordingly, applicants request reconsideration of the application, withdrawal of the objections and rejections of record and issuance of a Notice of Allowance.

Claims 1-39 are pending in the application. Claims 1-14, 20-24, 30 and 35-39 are rejected and Claims 15-19, 25-29, 31 and 32 are objected to for the reasons of record. Claims 33 and 34 have been withdrawn from consideration as being drawn to a non-elected amino acid sequence without prejudicing the right to file a divisional application thereon. Claims 1, 4, 5, 10, 15, 20, 25, 30, 31, 32 and 36 have been amended in response to the various objections noted on pages 3 and 4 of Paper No. 10. The amendments of the claims are not considered to involve the addition of new matter and entry of the amended claims is respectfully requested.

The disclosure is objected to because SEQ ID NOS were not inserted after every amino acid sequence in the application subject to the sequence disclosure rules as originally filed. The Examiner has required a substitute specification containing these additions, which is submitted herewith.

The Examiner has also noted that the sequence listing filed June 28, 2001 lists 210 sequences and that he could not find any sequences in the specification or claims with a SEQ ID NO higher than 202.

Applicants have identified these sequences as being ones that were not identified according to the sequence disclosure rules as noted above. Each of these sequences was in the application as originally filed without "SEQ ID NO" inserted thereafter. These have been inserted in the substitute specification according to the sequence disclosure rules. Additionally, new sequence numbers have been added in the application in response to the examiner's objections. A new sequence listing will be sent, along with a computer readable format, under separate cover.

Rejections Under 35 U.S.C. § 112, second paragraph

Claim 4-14, 20-24 and 30 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, in claim 4, the final R group is unclear because it contains bonds at both ends of the substituent. This is also found in Claims 5 and 30.

Also, Claims 4, 5 and 30 are indefinite because the term "or" needs to be inserted so that standard Markush terminology is used. Additionally, in Claims 5, 10 and 20, the word "and" should be inserted after the semicolon so that standard Markush terminology is used.

Finally, in Claim 10, the word "or" should be changed to "and" so that standard terminology is used.

Applicants have amended each of these claims in order to overcome the 112, 2nd paragraph rejections. The bond before the final R group in Claims 4, 5 and 30 has been removed as it is clearly an inadvertent typographical error.

Claims 1-19, 31 and 35-39 are objected to as containing various informalities. In Claims 1, 4 and 5, the examiner questions whether "α-Ala" should be "β-Ala" since "α-Ala" is ordinarily presumed from the previously recited "Ala".

In Claims 1, 4, 5 and 10, the examiner points out that the amino acid designation "Cba" is repeated.

In Claims 10, 15 and 31, the examiner points out that a comma or semicolon should be inserted at the end of a certain line and that in Claim 36, the word "administering" is misspelled.

Applicants have amended the aforementioned claims and portions of the specification to correct the abovementioned informalities. The examiner is correct that "α-Ala" should be "β-Ala" as claimed in Claims 5, 10, 15, 20 and 25. However, Claim 5, as originally filed, included "β-Ala" and not "α-Ala".

Rejections Under 35 U.S.C. § 102(b), 102(e) and 35 U.S.C. § 103(a)

The examiner has noted that instant claims 1-32 and 35-39 are deemed not to be entitled under 35 U.S.C. § 119(e) to the benefit of the filing date of provisional application 60.189,387 because the provisional application, under 35 U.S.C. § 112, 1st paragraph, does not disclose, e.g., all of the E^{cp} groups recited in the instant claims. The examiner notes that Trouet et al., U.S. Patent No. 5,962, 216 is therefore available as prior art against the instant claims under 35 U.S.C. § 102(b).

Applicants respectfully disagree that the subject claims are not entitled to the benefit of the provisional filing date. However, in view of the following remarks, Trouet et al. is not considered to be relevant prior art against the instant claims.

Claims 1 and 2 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Trouet et al. The examiner notes that Trouet et al. teach the prodrug compound Gly-Leu-Gly-Leu-DNR. This compound, the examiner notes, corresponds to Applicants' claimed compound in which E^{cp} is Cap-Gly-Xp1-Xp2-Laa where Cap is R, which is hydrogen. The examiner also notes that Applicants' claims permit Cap/R to be hydrogen because Claim 33, page 99, SEQ ID NO 8 has only hydrogen atoms at its N-terminus.

Applicants respectfully traverse this ground of rejection and present the following comments. Nowhere in the specification or claims is R defined as hydrogen. Cap is defined as an N-terminus group selected from R-, Xa4 and R-Xa4. In SEQ ID NO:8, the Cap is Xa4 defined as P (proline). Additionally, the specification clearly excludes compounds provided that E^{cp} is not –Gly-Leu-Gly-Leu-. (p. 36) Thus, the compound in Trouet et al does not correspond to Applicants' claimed compound in which E^{cp} is Cap-Gly-Xp1-Xp2-Laa.

In view of the foregoing, withdrawal of this ground of rejection is respectfully requested.

Claims 35-39 are rejected under 35 U.S.C. § 103 (a) as being obvious over Trouet et al. The examiner notes that the application of Trouet et al. is the same as in the 102(b) rejection of Claims 1 and 2. The examiner notes that while Trouet et al. does not teach administering the prodrug compound in combination with a pharmaceutically acceptable carrier in order to treat breast cancer/carcinoma, that it would be obvious to one of ordinary

skill in the art at the time Applicants' invention was made to use the prodrug of Trouet et al. to treat breast cancer/carcinoma. The examiner points out that it is desirable to treat such a disease and since Trouet et al. teaches that daunorubicin is released from its prodrug form by enzymes present in breast cancer/carcinoma cells, it would be obvious to one of ordinary skill in the art to administer the prodrug of Trouet et al. in combination with a pharmaceutically acceptable carrier since it is routine to administer therapeutic agent sin combination with pharmaceutically acceptable carriers for ease of storage, transportation, measurement and administration.

Applicants respectfully traverse this ground of rejection and provide the following comments. In view of the comments in response to the 102 (b) rejection, Applicants submit that since the compounds claimed in Claims 1 and 2 are novel, their use as claimed in Claims 35-39 would not be obvious over Trouet et al. Applicants submit that this ground of rejection should also be withdrawn.

Claims 1-14 are rejected under 35 U.S.C. § 103 (a) as being obvious over Trouet et as applied against Claims 1 and 2 above and further in view of WO Patent Application 00/64486. The examiner notes that Trouet et al. generally teach a terminal group Z (sic)(should be W), especially succinyl, linked through a peptide Z to a therapeutic agent M, especially doxorubicin. The peptide Z is cleaved by enzymes secreted by the target cells to permit entry of the therapeutic agents into the target cells. Trouet et al., it is clearly noted by the examiner, do not teach a peptide Z which is cleavable by a matrix metalloproteinase and which corresponds to Applicants' elected E^{cp} group. The '486 application teaches an amino acid sequence Pro-Leu-Gly-Leu-Trp-Ala which is cleaved by matrix metalloproteinases. The examiner notes that the amino acid sequence of the '486 application corresponds to Applicants elected E^{cp} group as defined in instant Claims 1, 4, 5 and 10. The examiner concludes that it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form the prodrugs of Trouet et al. using the amino acid sequence taught by the '486 application because Trouet et al's prodrugs can be formed using any peptide which is cleaved by an enzyme, and because the WO applications' amino acid sequence is described as being cleavable by an enzyme which is associated with the tumor cells which are to be treated by Trouet et al.

Applicants respectfully traverse the rejection and present the following comments. The elected E^{cp} group is Cap-Paa-Xa2-Gly-Xp1-Xp2-Laa-. The amino acid sequence taught in the '486 application does not correspond to Applicants' elected E^{cp} group. As argued above, R is not equal to H and as such takes the amino acid sequence taught in the '486 application outside the elected species. Additionally, in paragraph 0447 of the published specification of the instant application, it specifically excludes succinyl as a substituent for Cap. Thus, without this crucial link, there is no basis for combining the references in order to render obvious the instant claims.

Applicants submit that the instant claims are not obvious over Trouet et al. in view of the WO 0064486 application and request that this ground of rejection be withdrawn.

Claims 1-5 and 35-39 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Monsigny et al. (U.S. Patent No. 4,703,107). The '107 patent, the examiner notes, teaches anti-tumoral prodrugs PHA-Gly-Gly-L-Arg-L-Leu-Daunorubicin and PHA Gly-Gly L-Arg-L-Leu-Adriamycin. The drugs are liberated from the prodrugs by proteases excreted from the tumoral cells. It is also noted that the prodrugs can be combined with pharmaceutically acceptable carriers. The examiner points out that the prodrugs correspond to Applicants' claimed compound in which E^{cp} is Cap-Xa2-Gly-Xp1-Laa or Cap-Gly-Xp1-Xp2-Laa, where Cap is R, which is polyhydroxyalkanoyl.

Applicants respectfully traverse the rejection and present the following comments. In paragraph 0444 of the published specification of the instant application, it specifically excludes polyhydroxyalkanoyl as a Cap substituent. Clearly without this crucial piece, the '107patent cannot anticipate the instant claims. Applicants submit that this ground of rejection should be withdrawn.

Claims 1-14 and 35-39 are rejected under 35 U.S.C. § 102 (e) as being anticipated by Firestone et al. (U.S. 2002/0147138 A1). The examiner notes that Firestone et al. teach the enzyme activated anti-tumor and anti-metastatic prodrug N-Cbz-Gly-Phe-Ala-Leu-doxorubicin. The peptide portion is noted to be capable of being cleaved by collagenase (IV) or elastase. The prodrug, the examiner states, corresponds to Applicants' claimed compounds in which E^{cp} is Cap-Gly-Xp1-Xp2-Laa. The examiner goes on to note that in view of the similarity in structure between the peptide portion of the

prodrug of Firestone et al. and Applicants' claimed E^{cp} group, the prodrug of Firestone is deemed inherently to be cleavable by the matrixins specified in these claims. The examiner concludes that sufficient evidence of similarity is deemed to be present to shift the burden to Applicants to provide evidence that the claimed compounds are unobviously different than that of Firestone et al.

Applicants respectfully traverse the application and present the following comments. The examiner has "deemed" sufficient evidence of similarity is present in order to shift the burden to Applicants to provide evidence that the claimed compounds are not obvious in view of Firestone et al. The examiner has given no evidence of similarity to shift the burden. Nowhere in Firestone et al. is any mention made of a matrixin. Applicants submit that the examiner must provide more than mere conclusions to shift this burden of proof to Applicants

The examiner notes that Firestone et al. teach a particular prodrug containing N-Cbz as the amino protecting group. The instant application does not disclose the substituent "Cap" as being N-Cbz or any other protecting group. Cap is clearly defined as an N-terminus group selected from R-; Xa4-; and R-Xa4-. None of these can be N-Cbz in any occurrence. Clearly there is no anticipation of the compounds of the invention and clearly there is no evidence of similarity to shirt the burden to Applicant.

Applicants submit that the rejection under 35 U.S.C. § 102 (e) over Firestone et al. should be withdrawn.

Applicants acknowledge the examiner's comments that Claims 15-19 would be allowable if rewritten to overcome the claim objections set forth in the action and to include all of the limitations of the base claim and any intervening claims. Additionally, Claims 20-24 would be allowable if rewritten or amended to overcome the rejections under 35 U.S.C. § 112, 2nd paragraph, as set forth in the action. Claims 25-29 are also objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The examiner notes that the prior art of record does not teach or suggest E^{cp} groups having the particular combination of R groups and amino acid sequences required by these claims.

The examiner has also noted that Claims 30-32 limited to the elected SEQ ID NO would be allowable if rewritten to overcome either the rejections under 35 U.S.C. § 112,

2nd paragraph, the claims objections or if rewritten in independent form, respectively, and to include all of the limitations of the base claim and any intervening claims. It is acknowledged that the prior art of record does not teach or suggest an E^{cp} group having the structure of the elected SEQ ID NO.

Applicants will consider rewriting Claims 15-32 as suggested following the examiner's consideration of the arguments presented in this repsonse.

In view of the foregoing, Applicants submit that the application, as amended, is in condition for allowance and courteously solicit a Notice of Allowance.

If any fee due is not accounted for herein, please charge such fee to Deposit Account No. 19-3880. If any extension of time is required and not petitioned for, such extension is hereby petitioned for, and it is requested that any fee due in connection therewith be charged to the aforementioned Deposit Account.

Please contact the undersigned attorney on any matter relating to this application.

Respectfully submitted,

Elliott Korsen
for Applicants
Reg. No. 32,705

Date: March 28, 2003
Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000
(609) 252-4741

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claims:

Claim 1 (amended). A compound of Formula (I):

E^{cp}-A

(I)

or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide conjugated to A and selected from:

Cap- Paa -Xa2 -Gly - Xp1 - Laa -;

Cap- Xa2 - Gly - Xp1 - Laa -;

Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Laa -;

Cap- Xa2 - Gly - Xp1 - Xp2 - Laa -;

Cap- Gly - Xp1 - Xp2 - Laa -;

Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Gly - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Paa - Xa2 - Sar - Xp1 - Laa -;

Cap- Xa2 - Sar - Xp1 - Laa -;

Cap- Paa - Xa2 - Sar - Xp1 - Xp2 - Laa -;

Cap- Xa2 - Sar - Xp1 - Xp2 - Laa -;

Cap- Sar - Xp1 - Xp2 - Laa -;

Cap- Paa - Xa2 - Sar - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Xa2 - Sar - Xp1 - Xp2 - Xp3 - Laa -; and

Cap- Sar - Xp1 - Xp2 - Xp3 - Laa -;

Paa is a Pro, Hyp, Aze, homo-Pro, Chg, Fph, Npa, Tzc, or proline mimetic;

Xa2 is an amino acid;

Xp1 is an amino acid wherein -Gly-Xp1- or -Sar-Xp1- form a bond cleavable by a matrixin;

Xp2 is an amino acid;

Xp3 is an amino acid;

Laa is an amino acid selected from Leu, Ile, Nle, β-homo-Leu, Hol, Hos, Ala, [α]β-Ala, Cha, [Cba,]Cba, Cta, 4-pyridyl-Ala, 3-pyridyl-Ala, 2-pyridyl-Ala, Gly, Abu, Aib, Iva, Nva, Ahx, Aph, Amh, Phe, Bip, Glu, Arg, Trp, Tyr, O-(C_1-C_4 alkyl)-Tyr, O-(phenyl(C_1-C_4 alkyl)-)-Tyr, (C_3-C_8 alkyl)-Gly, and aminoalkyl carboxylic acid;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

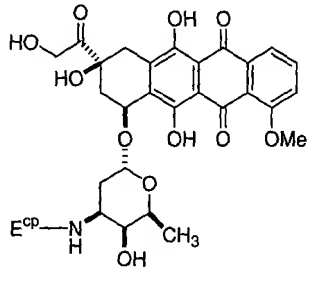
Xa4- is an amino acid;

R is an amino capping group;

and

A is an antineoplastic agent.

Claim 4 (amended). A compound of Claim 3 of Formula (Ia):



(Ia)

or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

Cap- Paa - Xa2 - Gly - Xp1 - Laa -;

Cap- Xa2 - Gly - Xp1 - Laa -;

Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Laa -;

Cap- Xa2 - Gly - Xp1 - Xp2 - Laa -;

Cap- Gly - Xp1 - Xp2 - Laa -;

Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Gly - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Paa - Xa2 - Sar - Xp1 - Laa -;

Cap- Xa2 - Sar - Xp1 - Laa -;

Cap- Paa - Xa2 - Sar - Xp1 - Xp2 - Laa -;

Cap- Xa2 - Sar - Xp1 - Xp2 - Laa -;

Cap- Sar - Xp1 - Xp2 - Laa -;

Cap- Paa - Xa2 - Sar - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Xa2 - Sar - Xp1 - Xp2 - Xp3 - Laa -; and

Cap- Sar - Xp1 - Xp2 - Xp3 - Laa -;

Paa is a Pro, Hyp, Aze, homo-Pro, Chg, Fph, Npa, Tzc, or proline mimetic;

Xa2 is an amino acid;

Xp1 is an amino acid wherein -Gly-Xp1- or -Sar-Xp1- form a bond cleavable by a matrixin;

Xp2 is an amino acid;

Xp3 is an amino acid;

Laa is an amino acid selected from Leu, Ile, Nle, β-homo-Leu, Hol, Hos, Ala, [α]β-Ala, Cha, Cba, [Cba,] Cta, 4-pyridyl-Ala, 3-pyridyl-Ala, 2-pyridyl-Ala, Gly, Abu, Aib, Iva, Nva, Ahx, Aph, Amh, Phe, Bip, Glu, Arg, Trp, Tyr, O-(C_1-C_4 alkyl)-Tyr, O-(phenyl(C_1-C_4 alkyl)-)-Tyr, (C_3-C_8 alkyl)-Gly, and aminoalkyl carboxylic acid;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid;

R is selected from: $H_3CC(=O)$-;

$HOC(=O)-(CH_2)_vC(=O)$-,

wherein v is 1, 2, 3, 4, 5, or 6;

$H_3CO-(CH_2CH_2O)_t-CH_2C(=O)$-,

$HO_2CCH_2O-(CH_2CH_2O)_t-CH_2C(=O)$-,

$H_2N-(CH_2CH_2O)_t-CH_2C(=O)$-, and

$H_3CC(=O)HN-(CH_2CH_2O)_t-CH_2C(=O)$-,

wherein t is 1, 2, 3, or 4;

$R^1-C(=O)$-;

R^1-S(=O)$_2$-;

R^1-NHC(=O)-;

R^{1a}-CH_2C(=O)-;

proline substituted with -OR^3;

C_1-C_4 alkyl substituted with 0-1 R^4;

2-carboxyphenyl-C(=O)-; and

[-](O=)C-phenyl-C(=O)-;

R^1 is C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from -OH, methoxy and -CO_2H;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH, methoxy or -CO_2H;

phenyl substituted with 0, 1, or 2 substituents selected from -OH, methoxy and -CO_2H; or

C_1-C_6 alkyl substituted with 0-4 R^{1a};

R^{1a} is -OH, C_1-C_3 alkyl, C_1-C_4 alkoxy, -CO_2H, -N(CH_2CH_2)$_2$N-R^2, -SO_3H;

C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

5-6 membered [hetereocycle]heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH; or

phenyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

R^2 is -H, H_2N(C_2-C_4 alkyl)-, acetyl(H)N(C_2-C_4 alkyl)-, or acetyl;

R^3 is -H, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, phenyl, or benzyl;

R^4 is -OH, C_1-C_3 alkyl, C_1-C_4 alkoxy, -CO_2H, -N(CH_2CH_2)$_2$N-R^2;

C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

5-6 membered [hetereocycle]heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH; or

C_6-C_{10} carbocycle substituted with 0, 1, or 2 substituents selected from methoxy and -OH.

Claim 5 (amended). A compound of Claim 4 of Formula (Ia), or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

Cap- Paa - Xa2 - Gly - Xp1 - Laa -;

Cap- Xa2 - Gly - Xp1 - Laa -;

Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Laa -;

Cap- Xa2 - Gly - Xp1 - Xp2 - Laa -;

Cap- Gly - Xp1 - Xp2 - Laa -;

Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;

Cap- Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -; and

Cap- Gly - Xp1 - Xp2 - Xp3 - Laa -;

Paa is a Pro, Hyp, Aze, homo-Pro, Chg, Fph, Npa, Tzc, or proline mimetic;

Xa2 is an amino acid;

Xp1 is an amino acid wherein -Gly-Xp1- forms a bond cleavable by a matrixin;

Xp2 is an amino acid;

Xp3 is an amino acid;

Laa is an amino acid selected from Leu, Ile, Nle, β-homo-Leu, Hol, Hos, Ala, β-Ala, Cha, Cba, [Cba,]Cta, 4-pyridyl-Ala, Abu, Aib, Iva, Nva, Phe, Bip, Tyr, and O-benzyl-Tyr; and

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid;

R is selected from: $H_3CC(=O)$-;

$HOC(=O)$-$(CH_2)_vC(=O)$-,

wherein v is 1, 2, 3, or 4;

H_3CO-$(CH_2CH_2O)_t$-$CH_2C(=O)$-,

HO_2CCH_2O-$(CH_2CH_2O)_t$-$CH_2C(=O)$-,

H_2N-$(CH_2CH_2O)_t$-$CH_2C(=O)$-, and

$H_3CC(=O)HN$-$(CH_2CH_2O)_t$-$CH_2C(=O)$-,

wherein t is 1, 2, or 3;

R^1-$C(=O)$-;

R^1-$S(=O)_2$-;

R^1-$NHC(=O)$-;

R^{1a}-$CH_2C(=O)$-;

proline substituted with -OR^3;

C_1-C_4 alkyl substituted with 0-1 R^4;

$HO_3SCH_2CH(NH_2)C(=O)$-;

2-carboxyphenyl-$C(=O)$-; and

[-](O=)C-phenyl-$C(=O)$-;

R^1 is C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from -OH, methoxy and $-CO_2H$;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH, methoxy or $-CO_2H$;

phenyl substituted with 0, 1, or 2 substituents selected from -OH, methoxy and $-CO_2H$; or

C_1-C_6 alkyl substituted with 0-4 R^{1a};

R^{1a} is -OH, C_1-C_3 alkyl, C_1-C_4 alkoxy, $-CO_2H$, $-N(CH_2CH_2)_2N$-R^2, $-SO_3H$;

C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

5-6 membered [hetereocycle]heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH; or

phenyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

R^2 is -H, $H_2N(C_2$-C_4 alkyl)-, acetyl(H)N(C_2-C_4 alkyl)-, or acetyl;

R^3 is -H, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, phenyl, or benzyl;

R^4 is -OH, C_1-C_3 alkyl, C_1-C_4 alkoxy, $-CO_2H$, $-N(CH_2CH_2)_2N-R^2$;

C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

5-6 membered [hetereocycle]heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH; or

C_6-C_{10} carbocycle substituted with 0, 1, or 2 substituents selected from methoxy and -OH.

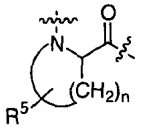
Claim 10 (amended). A compound of Claim 5 of Formula (Ia), or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

Cap- Paa - Xa2 - Gly - Xp1 - Laa -;
Cap- Xa2 - Gly - Xp1 - Laa -;
Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Laa -;
Cap- Xa2 - Gly - Xp1 - Xp2 - Laa -;
Cap- Gly - Xp1 - Xp2 - Laa -;
Cap- Paa - Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -;
Cap- Xa2 - Gly - Xp1 - Xp2 - Xp3 - Laa -; and
Cap- Gly - Xp1 - Xp2 - Xp3 - Laa -;

wherein -Gly-Xp1- forms a bond cleavable by a matrixin;

Paa is a Pro, Hyp, Aze, homo-Pro, Chg, Fph, Npa, Tzc, or proline mimetic of formula:



; wherein R^5 is selected from H, halogen, C_1-C_6 alkyl, -OH, C_1-C_6 alkoxy, and benzyloxy; and n is 2, 3, 4, or 5;

Xa2 is an amino acid selected from

Hof, Leu, His, Arg, Gln, Ile, Val, Lys, (R)-Leu, Orn, β-Ala, γ-Abu, Cha, Chg, Dap, Cit, N-methyl-Leu, valerolactam, N,N-dimethyl-Lys, 4-aza-Phe, morpholinylpropyl-Gly, N-methylpiperazinepropyl-Gly, 4-aza-Hof, Ala, Asn, Asp, Aze, Cys, Glu, Gly, Hyp, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Cya, Hca, and Spa;

Xp1 is an amino acid selected from Hof; Leu; Bip; Phe; nor-Leu; Tha; Phg; Val; Glu; Asn; Ser; Ala; homo-Tyr; Aze; 4-aza-Hof; O-(3-pyridyl)-Tyr; O-(4-pyridyl)-Tyr; O-benzyl-Tyr; O-benzyl-Thr; O-benzyl-Ser; O-methyl-Ser; O-allyl-Ser; 4-nitro-Hof; N-methyl-Leu; O-(4-pyridylmethyl)-Tyr; 4-hydroxy-phenyl-Gly; phenylpropyl-Gly; styryl-Ala, [or]and 2Nal;

Xp2 is an amino acid selected from Tyr; Ala; Ser; Leu; Gln; Val; Glu, His; Lys; Arg; Orn; Aze; Hof; homo-Tyr; Cit; 4-aza-Phe; N,N-[D]dimethyl-Lys; Dab; Dap; Asn, Asp, Aze, Cha, Cys, Gly, Hyp, Ile, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Thr, Trp, Cya, Hca, Spa, morpholinylpropyl-Gly; O-(4-pyridylmethyl)-Tyr; and N-methylpiperazinepropyl-Gly;

Xp3 is an amino acid selected from Tyr, Ala, Ser, Leu, Hof, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Thr, Trp, and Val;

Laa is an amino acid selected from Leu, Ile, Nle, β-homo-Leu, Hol, Hos, Ala, β-Ala, Cha, [Cba,]Cba, Cta, 4-pyridyl-Ala, Abu, Aib, Iva, Nva, and Phe;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid selected from Gly, Pro, γ-Glu, Dmg, Ala, Arg, Asn, Asp, β-Asp, Aze, Cha, Cys, Dpa, Gln, Glu, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Sar, Ser, Thr, Trp, Tyr, [or]and Val;

R is selected from: $H_3CC(=O)$-;

$HOC(=O)CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2CH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2C(=O)$- ;

$H_3COCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$HO_2CCH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_3CC(=O)HNCH_2CH_2OCH_2C(=O)$- ;

$H_3CC(=O)HNCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2N(CH_2CH_2)_2NCH_2C(O)$-;

$H_3CC(=O)HNCH_2CH_2N(CH_2CH_2)_2NCH_2C(O)$-;

$H_3CC(=O)N(CH_2CH_2)_2NCH_2C(O)$-;

$O(CH_2CH_2)_2NCH_2CH_2NHC(O)$- ;

$HO_2CCH_2C(CO_2H)(OH)CH_2C(=O)$- ;

$HO_2CCH_2C(CH_3)(OH)CH_2C(=O)$- ;

2-carboxycyclohexyl-C(=O)-;

2-carboxycyclopentyl-C(=O)-;

carbobenzyloxy;

4-methoxy-benzenesulfonyl;

cyclopropylcarbonyl;

cyclobutylcarbonyl;

3-pyridinecarbonyl;

2-pyrazinecarbonyl;

tetrazoleacetyl;

pivaloyl;

methoxyacetyl;

hydroxyproline; and

4-(2-(5,6,7,8-tetrahydronaphthenyl))butyl.

Claim 15 (amended). A compound of Claim 10 of Formula (Ia), or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

Cap- Paa - Xa2 - Gly - Leu - Laa -;

Cap- Paa - Xa2 - Gly - Hof - Laa -;

Cap- Xa2 - Gly - Leu - Laa -;

Cap- Xa2 - Gly - Hof - Laa -;

Cap- Paa - Xa2 - Gly - Leu - Xp2 - Laa -;

Cap- Paa - Xa2 - Gly - Hof - Xp2 - Laa -;

Cap- Xa2 - Gly - Leu - Xp2 - Laa -;

Cap- Xa2 - Gly - Hof - Xp2 - Laa -;

Cap- Gly - Leu - Xp2 - Laa -; and

Cap- Gly - Hof - Xp2 - Laa -;

wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by a matrixin;

Paa is a Pro, Hyp, Aze, homo-Pro, or Npa;

Xa2 is an amino acid selected from

Hof, Leu, His, Arg, Gln, Ile, Val, Lys, (R)-Leu, Orn, β-Ala, γ-Abu, Cha, Chg, Dap, Cit, N-methyl-Leu, valerolactam, N,N-dimethyl-Lys, 4-aza-Phe, morpholinylpropyl-Gly, N-methylpiperazinepropyl-Gly, 4-aza-Hof, Ala, Asn, Asp, Aze, Cys, Glu, Gly, Hyp, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Cya, Hca, and Spa;

Xp2 is an amino acid selected from Tyr; Ala; Ser; Leu; Gln; Val; Glu, His; Lys; Arg; Orn; Aze; Hof; homo-Tyr; Cit; 4-aza-Phe; N,N-[D]dimethyl-Lys; Dab; Dap; Asn, Asp,

Aze, Cha, Cys, Gly, Hyp, Ile, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Thr, Trp, Cya, Hca, Spa, morpholinylpropyl-Gly; O-(4-pyridylmethyl)-Tyr; and N-methylpiperazinepropyl-Gly;

Laa is an amino acid selected from Leu, Cha, Nle, and Hol;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid selected from Gly, Pro, γ-Glu, and Dmg;

R is selected from: $H_3CC(=O)$-;

$HOC(=O)CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2CH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2C(=O)$- ;

$H_3COCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$HO_2CCH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_3CC(=O)HNCH_2CH_2OCH_2C(=O)$- ;

$H_3CC(=O)HNCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2N(CH_2CH_2)_2NCH_2C(O)$-;

$H_3CC(=O)HNCH_2CH_2N(CH_2CH_2)_2NCH_2C(O)$-;

$H_3CC(=O)N(CH_2CH_2)_2NCH_2C(O)$-;

$O(CH_2CH_2)_2NCH_2CH_2NHC(O)$- ;

$HO_2CCH_2C(CO_2H)(OH)CH_2C(=O)$- ;

$HO_2CCH_2C(CH_3)(OH)CH_2C(=O)$- ;

2-carboxycyclohexyl-C(=O)-;

2-carboxycyclopentyl-C(=O)-;

carbobenzyloxy;

4-methoxy-benzenesulfonyl;

cyclopropylcarbonyl;

cyclobutylcarbonyl;

3-pyridinecarbonyl;

2-pyrazinecarbonyl;

tetrazoleacetyl;

pivaloyl;

methoxyacetyl;

hydroxyproline; and

4-(2-(5,6,7,8-tetrahydronaphthenyl))butyl.

Claim 20 (amended). A compound of Claim 15 of Formula (Ia), or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

Cap- Paa - Xa2 - Gly - Leu - Leu -;

Cap- Paa - Xa2 - Gly - Leu - Cha -;

Cap- Paa - Xa2 - Gly - Leu - Nle -;

Cap- Paa - Xa2 - Gly - Leu - Hol -;

Cap- Paa - Xa2 - Gly - Hof - Leu -;

Cap- Paa - Xa2 - Gly - Hof - Cha -;

Cap- Paa - Xa2 - Gly - Hof - Nle -;

Cap- Paa - Xa2 - Gly - Hof - Hol -;

Cap- Paa - Xa2 - Gly - Leu - Xp2 - Leu -;

Cap- Paa - Xa2 - Gly - Leu - Xp2 - Cha -;

Cap- Paa - Xa2 - Gly - Leu - Xp2 - Nle -;

Cap- Paa - Xa2 - Gly - Leu - Xp2 - Hol -;

Cap- Paa - Xa2 - Gly - Hof - Xp2 - Leu -;

Cap- Paa - Xa2 - Gly - Hof - Xp2 - Cha -;

Cap- Paa - Xa2 - Gly - Hof - Xp2 - Nle -; and

Cap- Paa - Xa2 - Gly - Hof - Xp2 - Hol -;

wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by a matrixin;

Paa is a Pro, Hyp, Aze, homo-Pro, or Npa;

Xa2 is an amino acid selected from

Hof, Leu, His, Arg, Gln, Ile, Val, Lys, (R)-Leu, Orn, β-Ala, γ-Abu, Cha, Chg, Dap, Cit, N-methyl-Leu, valerolactam, N,N-dimethyl-Lys, 4-aza-Phe, morpholinylpropyl-Gly, N-methylpiperazinepropyl-Gly, 4-aza-Hof, Ala, Asn, Asp, Aze, Cys, Glu, Gly, Hyp, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, and Tyr;

Xp2 is an amino acid selected from Tyr; Ala; Ser; Leu; Gln; Val; Glu, His; Lys; Arg; Orn; Aze; Hof; homo-Tyr; Cit; 4-aza-Phe; N,N-[D]dimethyl-Lys; Dab; Dap; Asn, Asp, Aze, Cha, Cys, Gly, Hyp, Ile, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Thr, Trp; morpholinylpropyl-Gly; O-(4-pyridylmethyl)-Tyr; and N-methylpiperazinepropyl-Gly;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid selected from Gly, Pro, γ-Glu, and Dmg;

R is selected from: $H_3CC(=O)$-;

$HOC(=O)CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2CH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2CH_2OCH_2C(=O)$-;

2-carboxycyclohexyl-C(=O)-;

2-carboxycyclopentyl-C(=O)-; and

tetrazoleacetyl.

Claim 25 (amended). A compound of Claim 15 of Formula (Ia), or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

Cap- Xa2 - Gly - Leu - Leu -;

Cap- Xa2 - Gly - Leu - Cha -;

Cap- Xa2 - Gly - Leu - Nle -;

Cap- Xa2 - Gly - Leu - Hol -;

Cap- Xa2 - Gly - Hof - Leu -;

Cap- Xa2 - Gly - Hof - Cha -;

Cap- Xa2 - Gly - Hof - Nle -;

Cap- Xa2 - Gly - Hof - Hol -;

Cap- Xa2 - Gly - Leu - Xp2 - Leu -;

Cap- Xa2 - Gly - Leu - Xp2 - Cha -;

Cap- Xa2 - Gly - Leu - Xp2 - Nle -;

Cap- Xa2 - Gly - Leu - Xp2 - Hol -;

Cap- Xa2 - Gly - Hof - Xp2 - Leu -;

Cap- Xa2 - Gly - Hof - Xp2 - Cha -;

Cap- Xa2 - Gly - Hof - Xp2 - Nle -; and

Cap- Xa2 - Gly - Hof - Xp2 - Hol -;

wherein -Gly-Leu- and -Gly-Hof- form a bond cleavable by a matrixin;

Xa2 is an amino acid selected from

Hof, Leu, His, Arg, Gln, Ile, Val, Lys, (R)-Leu, Orn, β-Ala, γ-Abu, Cha, Chg, Dap, Cit, N-methyl-Leu, valerolactam, N,N-dimethyl-Lys, 4-aza-Phe, morpholinylpropyl-Gly, N-methylpiperazinepropyl-Gly, 4-aza-Hof, Ala, Asn, Asp, Aze, Cys, Glu, Gly, Hyp, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, and Tyr;

Xp2 is an amino acid selected from Tyr; Ala; Ser; Leu; Gln; Val; Glu, His; Lys; Arg; Orn; Aze; Hof; homo-Tyr; Cit; 4-aza-Phe; N,N-[D]dimethyl-Lys; Dab; Dap; Asn, Asp, Aze, Cha, Cys, Gly, Hyp, Ile, Irg, Met, Phe, Phe(4-fluoro), Pro, Sar, Thr, Trp; morpholinylpropyl-Gly; O-(4-pyridylmethyl)-Tyr; and N-methylpiperazinepropyl-Gly;

Cap is an N-terminus group selected from R-; Xa4-; and R-Xa4-;

Xa4- is an amino acid selected from Gly, Pro, γ-Glu, and Dmg;

R is selected from: $H_3CC(=O)$-;

$HOC(=O)CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2CH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2CH_2OCH_2C(=O)$-;

2-carboxycyclohexyl-C(=O)-;

2-carboxycyclopentyl-C(=O)-; and

tetrazoleacetyl.

Please note that each of the SEQ ID NO designations below has been amended from SEQ. ID. NO: in order to put these in proper form according to 37 CFR 1.821(d).

Claim 30 (amended). A compound of Claim 4 of Formula (I), or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

SEQ ID NO: 185:	R-γ-E -P-Orn-G-Hof-E-L-;
SEQ ID NO: 186:	R-γ-E -P-L-G-(O-benzyl-S)-Y-L-;
SEQ ID NO: 187:	R -γ-E -P-L-G-(O-benzyl-S)-Y-Nle-;
SEQ ID NO: 188:	R -P-L-G-(O-benzyl-S)-Y-L-;
SEQ ID NO: 189:	R -P-L-G-(O-methyl-S)-Y-L-;
SEQ ID NO: 190:	R -P-L-G-(azaHof)-Y-L-;
SEQ ID NO: 191:	R -P-L-G-Hof-Y-L-;
SEQ ID NO:. 192:	R -P-L-G-Hof-E-L-;
SEQ ID NO: 193:	R -P-L-G-(O-benzyl-S)-Y-Nle-;
SEQ ID NO: 194:	R -P-L-G-(O-methyl-S)-Y- Nle -;
SEQ ID NO: 195:	R -P-L-G-(azaHof)-Y- Nle -;
SEQ ID NO: 196:	R -P-L-G-Hof-Y- Nle -;
SEQ ID NO: 197:	R -P-L-G-Hof-E- Nle -;
SEQ ID NO: 198:	R -P-L-G-(O-benzyl-S)-Y-Hol-;
SEQ ID NO: 199:	R -P-L-G-(O-methyl-S)-Y- Hol -;
SEQ ID NO: 200:	R -P-L-G-(azaHof)-Y- Hol -;

SEQ ID NO: 201: R -P-L-G-Hof-Y- Hol -;

and

SEQ ID NO: 202: R -P-L-G-Hof-E- Hol -;

R is selected from: $H_3CC(=O)$-;

$HOC(=O)$-$(CH_2)_vC(=O)$- ;

wherein v is 1, 2, 3, 4, 5, or 6;

H_3CO-$(CH_2CH_2O)_t$-$CH_2C(=O)$- ;

HO_2CCH_2O-$(CH_2CH_2O)_t$-$CH_2C(=O)$- ;

H_2N-$(CH_2CH_2O)_t$-$CH_2C(=O)$- ; and

$H_3CC(=O)HN$-$(CH_2CH_2O)_t$-$CH_2C(=O)$- ;

wherein t is 1, 2, 3, or 4;

R^1-$C(=O)$-;

R^1-$S(=O)_2$-;

R^1-$NHC(=O)$-;

R^{1a}-$CH_2C(=O)$-;

proline substituted with -OR^3;

C_1-C_4 alkyl substituted with 0-1 R^4;

2-carboxyphenyl-C(=O)-; and

[-](O=)C-phenyl-C(=O)-;

R^1 is C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from -OH, methoxy and $-CO_2H$;

5-6 membered heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH, methoxy or $-CO_2H$;

phenyl substituted with 0, 1, or 2 substituents selected from -OH, methoxy and $-CO_2H$; or

C_1-C_6 alkyl substituted with 0-4 R^{1a};

R^{1a} is -OH, C_1-C_3 alkyl, C_1-C_4 alkoxy, -CO_2H, -$N(CH_2CH_2)_2N$-R^2 , -SO_3H;

C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

5-6 membered [hetereocycle]heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH; or

phenyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

R^2 is -H, $H_2N(C_2$-C_4 alkyl)-, acetyl(H)N(C_2-C_4 alkyl)-, or acetyl;

R^3 is -H, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, phenyl, or benzyl;

R^4 is -OH, C_1-C_3 alkyl, C_1-C_4 alkoxy, -CO_2H, -$N(CH_2CH_2)_2N$-R^2 ;

C_3-C_6 cycloalkyl substituted with 0, 1, or 2 substituents selected from methoxy and -OH;

5-6 membered [hetereocycle]heterocycle; said heterocycle being saturated, partially saturated or unsaturated; said heterocycle containing 1, 2, 3, or 4 heteroatoms selected from N, O, and S; said heterocycle optionally substituted with 1 or 2 -OH; or

C_6-C_{10} carbocycle substituted with 0, 1, or 2 substituents selected from methoxy and -OH.

Please note that each of the SEQ ID NO designations below has been amended from SEQ. ID. NO: in order to put these in proper form according to 37 CFR 1.821(d).

Claim 31 (amended). A compound of Claim 30 of Formula (I), or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

SEQ ID NO: 185: R-γ-E -P-Orn-G-Hof-E-L-;

SEQ ID NO: 186: R-γ-E -P-L-G-(O-benzyl-S)-Y-L-;

SEQ ID NO: 187: R -γ-E -P-L-G-(O-benzyl-S)-Y-Nle-;

SEQ ID NO: 188: R -P-L-G-(O-benzyl-S)-Y-L-;

SEQ ID NO: 189: R -P-L-G-(O-methyl-S)-Y-L-;

SEQ ID NO: 190: R -P-L-G-(azaHof)-Y-L-;

SEQ ID NO: 191: R -P-L-G-Hof-Y-L-;

SEQ ID NO: 192: R -P-L-G-Hof-E-L-;

SEQ ID NO: 193: R -P-L-G-(O-benzyl-S)-Y-Nle-;

SEQ ID NO: 194: R -P-L-G-(O-methyl-S)-Y- Nle -;

SEQ ID NO: 195: R -P-L-G-(azaHof)-Y- Nle -;

SEQ ID NO: 196: R -P-L-G-Hof-Y- Nle -;

SEQ ID NO: 197: R -P-L-G-Hof-E- Nle -;

SEQ ID NO: 198: R -P-L-G-(O-benzyl-S)-Y-Hol-;

SEQ ID NO: 199: R -P-L-G-(O-methyl-S)-Y- Hol -;

SEQ ID NO: 200: R -P-L-G-(azaHof)-Y- Hol -;

SEQ ID NO: 201: R -P-L-G-Hof-Y- Hol -;

and

SEQ ID NO: 202: R -P-L-G-Hof-E- Hol -;

R is selected from: $H_3CC(=O)$-;

$HOC(=O)CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2CH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2C(=O)$- ;

$H_3COCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$HO_2CCH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_3CC(=O)HNCH_2CH_2OCH_2C(=O)$- ;

$H_3CC(=O)HNCH_2CH_2OCH_2CH_2OCH_2C(=O)$- ;

$H_2NCH_2CH_2N(CH_2CH_2)_2NCH_2C(O)$-;

$H_3CC(=O)HNCH_2CH_2N(CH_2CH_2)_2NCH_2C(O)$-;

$H_3CC(=O)N(CH_2CH_2)_2NCH_2C(O)$-;

$O(CH_2CH_2)_2NCH_2CH_2NHC(O)$- ;

$HO_2CCH_2C(CO_2H)(OH)CH_2C(=O)$- ;

$HO_2CCH_2C(CH_3)(OH)CH_2C(=O)$- ;

2-carboxycyclohexyl-C(=O)-;

2-carboxycyclopentyl-C(=O)-;

carbobenzyloxy;

4-methoxy-benzenesulfonyl;

cyclopropylcarbonyl;

cyclobutylcarbonyl;

3-pyridinecarbonyl;

2-pyrazinecarbonyl;

tetrazoleacetyl;

pivaloyl;

methoxyacetyl;

hydroxyproline; and

4-(2-(5,6,7,8-tetrahydronaphthenyl))butyl.

Please note that each of the SEQ ID NO designations below has been amended from SEQ. ID. NO: in order to put these in proper form according to 37 CFR 1.821(d).

32. A compound of Claim 30 of Formula (I), or a pharmaceutically acceptable salt form thereof, wherein;

E^{cp} is an enzyme cleavable peptide selected from:

SEQ ID NO: 185:	R-γ-E -P-Orn-G-Hof-E-L-;
SEQ ID NO: 186:	R-γ-E -P-L-G-(O-benzyl-S)-Y-L-;
SEQ ID NO: 187:	R -γ-E -P-L-G-(O-benzyl-S)-Y-Nle-;
SEQ ID NO: 188:	R -P-L-G-(O-benzyl-S)-Y-L-;
SEQ ID NO: 189:	R -P-L-G-(O-methyl-S)-Y-L-;
SEQ ID NO: 190:	R -P-L-G-(azaHof)-Y-L-;
SEQ ID NO: 191:	R -P-L-G-Hof-Y-L-;
SEQ ID NO: 192:	R -P-L-G-Hof-E-L-;

SEQ ID NO: 193: R -P-L-G-(O-benzyl-S)-Y-Nle-;

SEQ ID NO: 194: R -P-L-G-(O-methyl-S)-Y- Nle -;

SEQ ID NO: 195: R -P-L-G-(azaHof)-Y- Nle -;

SEQ ID NO: 196: R -P-L-G-Hof-Y- Nle -;

SEQ ID NO: 197: R -P-L-G-Hof-E- Nle -;

SEQ ID NO: 198: R -P-L-G-(O-benzyl-S)-Y-Hol-;

SEQ ID NO: 199: R -P-L-G-(O-methyl-S)-Y- Hol -;

SEQ ID NO: 200: R -P-L-G-(azaHof)-Y- Hol -;

SEQ ID NO: 201: R -P-L-G-Hof-Y- Hol -;

and

SEQ ID NO: 202: R -P-L-G-Hof-E- Hol -;

R is selected from: $H_3CC(=O)$-;

$HOC(=O)CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2C(=O)$-;

$HOC(=O)CH_2CH_2CH_2CH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2C(=O)$-;

$H_3COCH_2CH_2OCH_2CH_2OCH_2C(=O)$-; and

tetrazoleacetyl.

Claim 36 (amended). A method of treating a mammal afflicted with a cancer comprising [adminstering] <u>administering</u> to a mammal afflicted with a cancer a therapeutically effective amount of a compound of Claim 1.